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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/021,368	12/12/2001	Vimla Band	00398-100005	3165

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EXAMINER	
NASHED, NASHAAT T	
ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 12/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/021,368	BAND, VIMLA	
	Examiner	Art Unit	
	Nashaat T. Nashed	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 December 2001*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *69-81* is/are pending in the application.

4a) Of the above claim(s) *79-81* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *69-78* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

The application has been amended as requested in the communication filed December 12, 2001. Accordingly, claims 1-68 have been canceled, and claims 69-81 have been entered.

Claims 69-81 are pending.

Restriction to one of the following inventions is required under 35 U.S.C. 121:

Group I Claims 69-78, drawn to a diagnostic method for cancer and a kit comprising a nucleic acid encoding NES1 polypeptide, classified in Class 435, subclass 6.

Group II Claims 79-81, drawn to a a kit comprising a NES1 polypeptide, classified in Class 435, subclasses 219.

The inventions are distinct, each from the other because of the following reasons:

Inventions of Groups I and II are related as product and processes of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the method of Group I does not utilize the kit containing the NES1 polypeptide of Group I.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

During a telephone conversation with Lee Crews on October 24, 2003 a provisional election was made without traverse to prosecute the invention of Group I, claims 69-78. Affirmation of this election must be made by applicant in replying to this Office action. Claims 79-81 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 C.F.R. § 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 C.F.R. § 1.48(b) and by the fee required under 37 C.F.R. § 1.17(h).

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and

(a)(2), see for example see page 24, line 22 through page 25, line 2. Applicant is required to enter specific sequence identification number following a sequence or a reference to a specific sequence.

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 69-78 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 and 11-14 of U.S. Patent No. 6,153,387 (387'). Although the conflicting claims are not identical, they are not patentably distinct from each other. Claims 11-144 of the 387' patent are directed to a diagnostic method for detecting malignancy or an increased likelihood of developing a malignancy in a patent using the nucleic acid sequence of SEQ ID NO: 2. Claim 69 of the instant application differes only in scope from claim 11 of the 387 and the embodiment of said claim 11 would be covered by claim 69 of the instant application if claim 69 found allowable. The word kit does not distinguish claims 77 and 78 from claims 1-4 of the 387' directed to the nucleic acid sequenc encoding the NES1 polypeptide.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly

connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 69-78 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 69-76 are directed to a method of detecting carcinoma or an increases likelihood of developing carcinoma by examining the level of expression or mutation in a NES1 gene which is down regulated in transformed epithelial cells. Claims 77 and 78 are directed to a composition comprising all possible NES1 genes. The specification, however, only provides a single representative species from human cell lines, i. e., the NES1 gene of SEQ ID NO: 2. There is no disclosure of any particular structure to function/activity relationship in the single disclosed species. The specification also fails to describe additional representative species of these NES1 gene by any identifying structural characteristics or properties other than being down regulated in transformed cells, for which no predictability of structure is apparent. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Claim 75 is directed to a method of detecting carcinoma or an increases likelihood of developing carcinoma by examining the level of expression of the NES1 polypeptide by assaying NES1 protein expression or activity. While the specification describe general methodology for assaying serine proteases using thiobenzylesters of amino acids, see page 31 second paragraph, the specification fails to teach a specific thiobenylester of any amino acid or peptide which is hydrolyzed by the polypeptide of SEQ ID NO: 1, let alone, all other gene products of the NES1 genes. Also, the specification has failed to teach whether the NES1 protein is an exo- or an endopeptidase. If the NES1 is an endopeptidase, it is possible that none of the thiobenzylesters could be a substrate for the NES1 protein activity. In addition, it should be noted that thiobenzylesters are chemically reactive compound toward hydrolysis. In the event, they are found to be substrate for the NES1 polypeptide, they would be expected to be non-specific substrates for the NES1 polypeptide. Thus, assaying the natural level of NES1 polypeptide in biological fluids which contain many proteases of all kind using a non-specific substrate is not feasible.

Claim 69-78 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to NES1 gene of SEQ ID NO: 2 from human. The specification does not enable any person skilled in the art to make and use the invention commensurate in scope with this claim. The claims are broader than the enablement provided by the

disclosure with regard to the large number of all possible NES1 gene from any mamal that are expressed in normal cells but not in transformed cells. Factors to be considered in determining whether undue experimentation is required, are summarized *In re* Wands [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

The nature and breadth of the claimed invention encompasses any composition comprising a gene encoding NES1 polypeptide from any mammalian source, said gene is expressed in normal epithelial cells, but not in transformed epithelial cells and their mutants (claims 77 and 78). Also, the claims are directed to all possible insertion, deletion, substitution and combination thereof mutants. Claims 69-76 is directed to a dignostic method to detect cancer in mammals. The specification provides guidance and examples in the form of an assay to characterize the NES1 gene having the nucleotide sequence of SEQ ID NO: 2 encoding the polypetide of SEQ ID NO:1, and relating it to epithelial cell transformation. Also, it suggests that the NES1 polypeptide is a serine protease. While molecular biological techniques and genetic manipulation to make the protein of SEQ ID NO:1 are known in the prior art and the skill of the artisan are well developed, knowledge regarding all types of NES1 proteins, the link between cell transformation and particular protein, and mutation on the activity or functionality of a protein or an enzyme is lacking. The specification teaches that NES1 polypeptide of SEQ ID NO: 1 is down regulated only in transformed epithelial cell from breast and cervical tumor isolated from female subjects. Thus, searching for a NES1 gene which is down regulated due to any mammalian cell transformation which may or may not have a serine protease activity an d/or mtants therof is well outside the realm of routine experimentation and predictability in the art of success in finding it is extremely low. The amount of experimentation to identify a NES1 protein or its mutants with such a characteristics is enormous. Since routine experimentation in the art does not include screening for numbers of genes in genomic and cDNA libraries, proteins, enzymes, polypeptides, peptides, and their mutants where the expectation of obtaining the desired NES1 protein is unpredictable, the Examiner finds that one skilled in the art would require additional guidance, such as information regarding the gene sequence being down regulated and its biological source, the mechanism of down regulation, the transforming agent, a specific chemical assay method, and the link between down regulation of a particular protein and transformation. Without such guidance, the experimentation left to those skilled in the art is undue.

Claims 69-78 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following are the reasons for the rejections:

(a) claims 69, 74, 75, 77, and 78 contain the undefined abbreviation NES1. Abbreviations must be defined at least once in the claims. For examination purposes only, NES1 is presumed to mean "Normal Epithelial Specific 1".

(b) claims 69, 74, 75, 77, and 78 contain the term NES1 which renders the claims indefinite because the resulting claims do not clearly set forth the metes and bounds of the patent protection desired. The term NES1 could either refer to the oligopeptide of SEQ ID NO: 1 or any other seine protease that is expressed in normal mammalian cells but not in transformed tumor cells. In examining the claims, the Examiner assumes that NES1 is any protein that is expressed in normal cells but not in transformed cell.

(c) The phrase "NES1 protein ..... or activity" renders the claims indefinite because the resulting claims do not clearly set forth the metes and bounds of the patent protection desired. The specification does not define NES1 protein activity and one of ordinary skill in the art would not what it is. For examination purposes only, the phrase is taken to mean a "serine protease activity" which also indefinite phrase.

(d) Claims 70-73 and 76 are included with this rejection because they are dependent on a rejected claim and do not cure its deficiencies.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nashaat T. Nashed, Ph. D. whose telephone number is (703) 305-6586. Effective January 22, 2004, the examiner telephone number will be changed to 571-272-0934. The examiner can normally be reached Monday, Tuesday, Thursday and Friday from 9:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached on (703) 308-3804. The fax phone numbers for this Group are (703) 305-3014 and (703)308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Nashaat T. Nashed, Ph. D.
Primary Examiner